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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/658,862	09/08/2000	Keith Henry Stockman Campbell	SP-02-US-DIV-1	2555

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EXAMINER	
CROUCH, DEBORAH	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/658,862	STOCKMAN CAMPBELL ET AL.	
	Examiner	Art Unit	
	Deborah Crouch, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2008 and 13 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *163 and 168-171* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *163 and 168-171* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/803,165.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

A request for continued examination under 37 CFR 1.114 was filed in this application after a decision by the Board of Patent Appeals and Interferences, but before the filing of a Notice of Appeal to the Court of Appeals for the Federal Circuit or the commencement of a civil action. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on June 13, 2008 has been entered. The amendment filed March 30, 2008 has been entered. Claims 163 and 168-171 are pending. The declaration by Irina A. Polejaeva, Ph.D. filed March 30, 2008 has been considered but is not persuasive for the reasons given below.

Applicant has previously filed proper terminal disclaimers regarding U.S. Patents 6,137,276; 6,252,133 and 6,525,243. The present claims are still seen as obvious over these patents. However, an obviousness-type double patenting rejection was not made since terminal disclaimers had been filed and approved.

Applicant's amendment to the claims has overcome the statutory type (35 U.S.C. 101) double patenting rejection made in the Examiner's Answer mailed September 12, 2006.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA

1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 163 and 170 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 11 and 12 of U.S. Patent 7,232,938; claims 1-9, 11-20 and 22 of U.S. Patent No. 7,304,204; claims 17 and 18 of U.S. Patent 7,307,198; claims 1-3 and 10 of U.S. Patent 7,321,076; claims 1, 2, 7-9, 14 and 191 of U.S. Patent 7,326,824; claims 1, 6-11 and 16-20 of U.S. Patent 7,326,825; claims 12 and 14 of U.S. Patent No. 7,332,648; claims 1, 6-11, 16-20 of U.S. Patent 7,355,094; and claims 17-32 of U.S. Patent No. 7,361,804. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because the presently claimed cloned horses are a species produced by the methods of cloning ungulates claimed in the above mentioned patents.

Present claims 163 and 170 are directed to cloned horses made by a general method of nuclear transfer. The present specification discloses donor cells as being diploid, differentiated, somatic cells in the G0 or G1 phase of the cell cycle.

Claims 1, 2, 11 and 12 of U.S. Patent 7,232,938; claims 1-9, 11-20 and 22 of U.S. Patent No. 7,304,204; claims 17 and 18 of U.S. Patent 7,307,198; claims 1-3 and 10 of U.S. Patent 7,321,076; claims 1, 2, 7-9, 14 and 191 of U.S. Patent 7,326,824; claims 1, 6-11 and 16-20 of U.S. Patent 7,326,825; claims 12 and 14 of U.S. Patent No. 7,332,648; claims 1, 6-11, 16-20 of U.S. Patent 7,355,094; and claims 17-32 of U.S. Patent No. 7,361,804 are directed to methods of producing cloned nonhuman ungulates using donor cells in the G0 or G1 phase of the cell cycle.

Thus, at the time of the instant invention, it would have been obvious to the ordinary artisan to arrive at the presently claimed horse given the methods claimed in any of the above mentioned patents.

Claims 163 and 170 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 27, 32-34, 43 and 48-50 in U.S. application serial no. 11/543,786 and claims 19, 24-26, 35 and 40-42 in U.S. application serial no. 11/544,038. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645

(Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because the presently claimed cloned horses are a species produced by the methods of cloning ungulates claimed in the above mentioned patents.

Present claims 163 and 170 are directed to a live-born clone of a pre-existing, non-embryonic donor horse. The present specification discloses donor cells as being diploid, differentiated, somatic cells in the quiescent, G0 or G1 phase of the cell cycle.

Claims 27, 32-34, 43 and 48-50 in 11/543,786 are directed to an ungulate reconstituted, single cell embryo comprising a quiescent ungulate cell or its nucleus. Claims 19, 24-26, 35 and 40-42 of 11/544,038 are to an ungulate reconstituted single cell embryo comprising a diploid ungulate differentiated cell or its nucleus. The embryos are disclosed as being transferred to a female for term development.

Thus at the time of the instant invention it would have been obvious to the ordinary artisan to produce the cloned horse of the present claims given the reconstituted embryos of the claims in '786 or ‘038.

Claims 163 and 168-171 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 40-55 of copending Application No. 11/068,903. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of ‘903 are generic to the present claims.

Present claims 163 and 170 are directed to a live-born clone of a pre-existing, non-embryonic donor horse. The present specification discloses donor cells as being diploid, differentiated, somatic cells in the quiescent, G0 or G1 phase of the cell cycle.

Claims 40-55 of '903 are directed to methods of preparing a nonprimate mammalian embryo or nonprimate mammal comprising inserting the nucleus of a cultured diploid differentiated nonprimate mammalian nuclear donor cell into an unactivated, enucleated metaphase II-arrested nonprimate mammalian oocyte, activating the resulting embryo and developing the activated embryo to term.

Thus at the time of the instant invention, it would have been obvious to the ordinary artisan to produce the cloned horses of present claims 163 and 170 given the methods of claims 50-55 of '903.

These are provisional obviousness-type double patenting rejections because the conflicting claims have not in fact been patented.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 163 and 168-171 remain rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter for reasons set forth in the Examiner's Answer mailed September 12, 2006 and the BPAI Decision, mailed January 30, 2008. Claims 163 and 168-171 are drawn to a live born clone of a pre-existing, non-embryonic, donor mammal, wherein the mammal is selected from mice, rabbits, horses and rats. However, the claimed mammals do not sufficiently distinguish over pre-

existing mice, rabbits, horses and rats. Neither the claims nor the specification point out any structure or phenotype that separates cloned mice, rabbits, horses and rats from pre-existing mice, rabbits, horses and rats. The method of making the mammals does not imbue any new or novel characteristic to the cloned mammals nor does the method imbue a new use to the mammals claimed. Further, the claims clearly state that the clone is a copy of a pre-existing mammal. Hence, the mammal as claimed is indistinguishable from the mammal as found in nature. Thus, the cloned mice, rabbits, horses and rats of the claims is not seen as being “new” as required by 35 U.S.C. § 101.

It is well known and accepted that patentability is precluded for certain subject matter, products of nature, natural phenomenon, being one of them. The claimed cloned mice, rabbits, horses and rats were, as disclosed in the specification, indeed, produced by a method that has the hand of man associated with it. However, the question raised under 35 U.S.C. § 101 relates to the patentability of subject matter that occurs in nature, is a copy of a product of nature, but the copy was created by the hand of man. Does the hand of man extend through the method to the product?

The actuality is, applicant developed a method whereby an embryo can be made by an in vitro method, and the embryo is transferred to a surrogate female nonhuman mammal. The surrogate female nonhuman mammal actually “makes" a cloned nonhuman mammal from applicant's in vitro produced embryo. By virtue of "employing" the naturally occurring female to produce the clone, a copy or replica of a prior existing mammal, the resultant mammal is a product of nature. In this regard, a mouse, rabbit,

horse and rat produced by IVF is a product of nature, even though the embryo was made in vitro through the hand of man. There are no structural differences between a mouse, rabbit, horse or rat produced by mating, IVF or cloning, at least none are disclosed in specification or recognized in the art.

Since there is no alteration of the cloned nonhuman mammals claimed versus nonhuman mammals produced by other means, cloned a mouse, rabbit, horse and rat cannot be distinguished from its IVF or mating produced counterpart. Without a distinction, each cloned mouse, rabbit, horse and rat is a product of nature. As detailed below, applicant's evidence and arguments are not persuasive.

To reiterate, the cloned mice, rabbits, horses and rats of the claim have not been described by the specification or the art as having any distinguishing effect by the hand of man method of making them. Thus, while applicant has a method that exhibits clearly the hand of man, it is not clear than the mammal products of the method exhibit the hand of man. Applicant, it would appear has invention a new method to produce a product of nature, similar to the IVF situation. There is no case law, other decisional law or policy that directs the patentability of fundamentally wild-type mice, rabbits, horses and rats produced by in vitro methods.

With regard to the BPAI instituted rejection, applicant argues "new" in 35 U.S.C. § 101 is not ignored. Applicant argues the cloned mice, rabbits, horses and rats are "new" because it does not exist in nature, but is made by man. Applicant continues in stating, in view of the BPAI's anticipation analysis, the clones are patentable because none of the references disclose exactly what is claimed. Applicant argues anticipation is

not shown by prior art disclosure which only "substantially" is the same as the claimed invention. Applicant argues the identical invention must be shown in the prior art in as complete detail as is contained in the claim. Applicant argues any difference precludes anticipation as established by legal precedent. Applicant argues differences between the claimed clones and their parents have been set forth in the declaration of David Wells previously filed, and the concurrently filed declaration by Irina A. Polejaeva, Ph.D. at parag. 92-110. These arguments are not persuasive.

35 U.S.C. § 101 states “Whoever invents or discovers any *new* and useful process, machine, manufacture, or composition of matter, or any *new* and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.” What permeates the prosecution of this application is how to distinguish the cloned mice, rabbits, horses and rats, *new* according to applicant, from mice, rabbits, horses and rats known in nature. There is no way to distinguish them, or at least none have been set forth. The cloned mice, rabbits, horses and rats look the same, behave the same, have the same chromosome number, same proteins, same physiology, same biochemistry, and they are used for same purposes. Their *newness* is not apparent. Applicant argues the clones are *new* in a 101 sense because of the method of making them, but applicant never states what the *new* is. A new way of making a product does not give the product "new" features necessarily. The method could provide new features to the product, but in the present prosecution no new features, characteristics, structure have been provided.

While it can be agreed upon, the clone and the nucleus donor mice, rabbits, horses and rats will have differences. Some differences will be caused by epigenetic differences, others by genetic differences. This is true for all animals. However, the differences have not been stated, nor has the effect of the differences been shown to make the clone "new." A clone could have crooked horn, the donor, a curved horn. A clone could have a white star on its muzzle; the donor have an all black muzzle. Yes, these are differences, but do they make the clone new, or do they make the clone statutory subject matter. The clone doesn't have a new use by having a crooked horn or a white star on its muzzle. It still functions the same as the donor mammal. How the clone is new and statutory is not clear from the specification, the art or the prosecution history. Applicant is attempting to establish newness by alluding to uncontrollable events that have no effect on the use of the clone. Given applicant's line of reasoning, a goat with a white coat is patentably distinct from a goat with a black coat. Coat color, marking and horns are not affected by the cloning method. The specification does not identify any step in the cloning method as regulating any structural characteristic of the clone. Thus, the characteristics the BPAI labeled as trivial are the differences that have no effect on the substance of the cloned mice, rabbits, horses or rats over the nuclear donor mice, rabbits, horses or rats.

Declarant Polejaeva states (parag. 94-110, pages 17-19) her opinion as to the differences between a clone and the nuclear donor mammal. Declarant states: parag. 90. Based on my experience cloning mammals, Applicant's clone is not made by nature; parag. 91. Based on my experience cloning mammals, Applicant's clone can only be

made by human intervention; parag. 92. Based on my experience cloning mammals, Applicant's clone is not an exact copy of its donor mammal; parag. 93. Based on my experience in mammalian reproduction, environmental factors would generate differences between Applicant's clone and its donor mammal; parag. 94. Based on my experience cloning mammals, Applicant's clone could not exist before it was made; parag. 95. Based on my experience cloning mammals, Applicant's clone occupies different space and time than its donor mammal, and is a time-delayed, inexact copy of its donor mammal. The clone contains the same genetic complement as its donor mammal, but is not an exact copy due to environmental differences during development; parag. 96. The ability of Applicant's clone to exist at a time later than its donor mammal, but have the same genetic complement, is a markedly different characteristic from any mammal found in nature; parag. 97. Based on my experience in mammalian reproduction, no mammal found in nature is a time-delayed copy of either of its parents; parag. 98. Based on my experience cloning mammals, Applicant's clone provides an alternative, time-delayed source of nuclear genomic material of its donor mammal; parag. 99. Based on my experience cloning mammals, this feature of Applicant's clone does not depend on the continued existence of the donor mammal; parag. 100 Consequently, Applicant's clone can provide an alternative source of nuclear genomic material of its donor mammal, even if the donor mammal is dead; parag. 101. The time delay of Applicant's clone allows the preservation of the genomic material of a particular mammal beyond the normal lifespan of that mammal; parag. 102. Normally, when a mammal dies, its particular genomic composition is lost. Its progeny only

contain one-half of each of its two parents' genomic material. The genomic material of one parent is inextricably scrambled together with the other parent's genomic material to create the progeny; parag. 103, Based on my experience cloning mammals, Applicant's clone avoids this permanent loss of a particular genomic composition; parag. 104. Thus, Applicant's clone provides the potential for the continuation of a particular genomic composition in a way that never occurs in nature; parag. 105. Based on my experience cloning mammals, this cannot be considered a trivial difference as compared to a clone's donor mammal, which does not have this potential; and parag.106. Moreover, Applicant's clone requires two animals, namely, a pre-existing, non-embryonic, donor mammal and a clone of that donor mammal. Based on my experience in mammalian reproduction, nature never makes such a pair of mammals. Declarant's statements are not persuasive.

Each of declarant's statements is an outcome provided by the method of nuclear transfer disclosed in the specification. There is no evidence that being a time-delayed clone of a mammal provides any feature to indicate the hand of man. Further, there is no evidence on record, in the specification or by declarant of any structural feature to a clone that indicates the hand of man. What is the aspect of the method that removes the cloned nonhuman mammal from the realm of non-statutory? Applicant seems to have invented a new method of producing a non-statutory class of invention.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to

> which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 163 and 168-171 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for reasons set forth in the Examiner's Answer mailed September 12, 2006. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

At the time of filing, the skilled artisan would have regarded the cloning of mice, rabbits, horses and rats to be unpredictable. Each used method steps not taught by the present specification.

The invention is the reproduction of pre-existing non-embryonic mice, rabbits, horses and rats by nuclear transfer, or cloning. Nuclear transfer methods require the insertion of a somatic cell or the nucleus of a somatic cell, referred to as the donor nucleus, into an enucleated oocyte, referred to as the recipient cell. If the recipient cell has not been activated prior to the insertion, the cell is activated post-insertion. The enucleated oocyte containing the donor nucleus is referred to as a reconstituted embryo. Although, the methods can vary, the reconstituted embryo is permitted to develop in vitro to the blastocyst stage, and the blastocyst is transferred to the uterus of a surrogate female of the same species as the donor nucleus and recipient oocyte for term development. Dolly, the first mammal cloned by somatic cell nuclear transfer (SCNT), is the most famous of mammalian clones. Dolly was produced by insertion of a nucleus of a sheep mammary gland epithelial cell into a sheep enucleated oocyte. As

stated by Campbell, out of 29 transferred reconstructed embryos, only one developed to produce a live lamb (Campbell (1997) Nature, page 811, Table 1). This evidence supports the argument SCNT was neither predictable nor routine at the time of filing.

At the time of filing, the skilled artisan would have regarded the cloning of mice, rabbits, horses and rats to be unpredictable. Each of the references discussed used method steps not taught by the present specification in the successful SCNT production of cloned mice, rabbits, horses and rats.

Nuclear transfer in rabbits was successful only when surrogate females were asynchronous by 22 hours from recipient oocytes (Chesne, page 366, col. 1, parag. 1, lines 10-13 and page 367, col. 2, parag. 1). In reporting the birth of a cloned horse, Galli states that the success was aided by advances in assisted reproduction in the horse, including oocyte activation, inhibition of both protein synthesis and protein phosphorylation and zona-free manipulation (Galli, page 635, col. 2, parag. 1, lines 7-13). Fitchev states that reconstituted rat embryos were transferred to the uterus of surrogate mothers but none developed to term (Fitchev, page 1528, col. 1, parag. 1, lines 1-3). The problem with rat somatic cell nuclear transfer is due to the spontaneous activation of rat oocytes within 30 minutes of their removal from the oviduct (Zhou, page 1179, col. 1, parag. 2, lines 5-10). Even when a “speedy” enucleation and transfer method was developed, no clones were born (Zhou, col. 2, lines 3-6 and parag. 1, lines 4-7). Successful cloning was reached when MG132, a protease inhibitor that reversibly blocks the first meiotic metaphase-anaphase transition in rat (Zhou, col. 2, parag. 2, lines 10-13). The method used in cloning mice included a prolonged interval between

nuclear injection and oocyte activation, suppressing cytokinesis (Wakayama, page 373, lines 1-4). Each method for cloning rabbits, horses, rats and mice used steps materially different and separate from that disclosed in the specification. As the specification does not provide any guidance to the cloning of these species per se, and the ultimate methods were materially different and lacked basis in the specification, the skilled artisan at the time of filing could not have relied upon the present specification to clone rabbits, horses, rats or mice. Thus, the skilled artisan would have needed to conduct an undue amount of experimentation without a predictable degree of success to implement the claimed invention.

The specification teaches a method of nuclear transfer, where the donor cell is in the G1 stage (specification, page 4, lines 2-4; and page 5, lines 20-24). The specification discloses the method would be useful in the cloning of mammals in general, and specifically discloses cattle, sheep, pig, goat, mouse, rabbit, horse and rat (specification, page 5, lines 16-24) The specification specifically teaches the production of sheep reconstructed embryos by nuclear transfer using a quiescent embryonic cell as the nuclear donor (specification, page 27, lines 6-12). Of ten transferred embryos, one live lamb was produced (page 28, Table 5, and lines 4-9). This example is not relevant to the claims as the donor cell in the example is an embryonic cell and the claims specifically require the donor to be a non-embryonic mammal. In view of the guidance in the specification and the art at the time of filing, it would have required an undue amount of experimentation without a predictable degree of success to clone by SCNT the claimed mice, rabbits, horses and rats. The specification at the time of filing, in view

of teachings in the art also at that time, provide evidence that sufficient guidance was not available for the cloning by SCNT of mice, rabbits, horses and rats.

Applicant argues Declarant Polejaeva explains cloning is an inefficient process and a large number of oocytes may be needed to be reconstructed to achieve success (parag. 19-21 and 75-77). Applicant argues declarant states the problem for many laboratories is manpower and financial resources to support a sufficiently large reconstruction effort. Declarant argues one way to maximize resources is to increase the efficiency of the cloning process. Applicant argues Declarant states increases efficiency is not required for successful cloning, but a method to increase the overall number of reconstructed embryos transferred to recipients. Applicant argues Declarant states successful cloning of previously reported cloned species are not usually publication worthy. Applicant argues Declarant states successful cloning is virtually guaranteed by reconstructing a sufficient number of nuclear transfer embryos. These arguments are not persuasive.

The specification offers no guidance as to improving the cloning of mice, rabbits, horses and rats, and certainly no guidance on what appears to be a "numbers game." The specification does not disclose any of the particular deviations from the claimed method used in the successful SCNT production of mice, rabbits, horses and rats. No where does the specification lead to the improvements of applicant's method that permitted the cloning of these species. Further applicant and declaration do not offer any evidence that these methods were routine or known in the art at the time of filing as useful in SCNT, or ECNT (embryonic cell nuclear transfer). There is no guidance for

the asynchronous transfer of reconstructed rabbit embryos to the surrogate female rabbit for term birth (Chesne, page 366, col. 1, parag. 1, lines 10-13 and page 367, col. 2, parag. 1); activation of horse oocytes, inhibition of both protein synthesis and protein phosphorylation and zona-free manipulation to produce a term foal (Galli, page 635, col. 2, parag. 1, lines 7-13); the inhibition of spontaneous activation of rat oocytes by incubation in a protease inhibitor (Zhou, page 1179, col. 1, parag. 2, lines 5-10); or a prolonged interval between nuclear injection and oocyte activation to suppress cytokinesis in mice embryos for the production of cloned mice (Wakayama, page 373, lines 1-4). Each of these art taught methods are not disclosed in the present specification specially nor are any of them suggested generally. Thus, each of these methods is an improvement to the method of the present specification, but the improvements have no basis in the specification. While declarant may be correct in stating efficiency needs to be improved to produce enough reconstructed embryos to transfer, there is no guidance in the specification for these specific improvements. There is no evidence that without these improvements success could have been reached at the time of filing in any of these species. In each reference cited, the authors are clear that they are the first to successful perform SCNT in mice, rabbit, horse and rat species. Thus, the methods of the present specification are not workable without the specific additions taught in the art, and applicant has offered no evidence to the contrary.

Applicant argues Declarant Polejaeva states (parag. 87) that the failure to produce cloned pigs between 1997 and 2000 was likely due to these laboratories reconstructing and/or implanting insufficient embryos to maintain pregnancy, and the

failures could have been remedied by reconstructing and transferring more nuclear transfer embryos to each surrogate pig. Applicant continues by arguing Fitchev is a good example of not reconstructing and transferring sufficient embryos to ensure success. Applicant argues Fitchev places the reconstructed embryos in the reproductive tracts of surrogate mother rats but none were successfully recovered. Applicant argues Fitchev, in transferring five embryos, did not transfer a sufficient number to obtain term birth. Applicant argues Declarant Polejaeva. These arguments are not persuasive.

Declarant's comments regarding the need to transfer a sufficient number of SCNT embryos is limited to pigs. In pigs, it was known in the art at the time of filing that to maintain implantation a female pig needed to have several, more than 4, embryos implanted into the uterus. Otherwise, the pregnancy was naturally terminated. (See). Thus, nuclear transfer in pigs was benefit by years of embryo transfer studies. However, pigs are not subject matter in the present set of claims; only mice, rabbits, horses and rats are present subject matter. Thus, applicant's arguments are not persuasive because they are directed to subject matter not of the claims. Further, there is no evidence that Fitchev's method would have been successful had more than 5 rat embryos been transplanted. Applicant has provided no evidence to support this argument. It could be that Fitchev's method was flawed in another step. All we can tell from Fitchev is nuclear transfer in rats was unpredictable, and could not be predictably obtained following applicant's method. Additionally, Declarant Polejaeva never addresses Fitchev directly. Fitchev, as cited above, states rat oocytes spontaneously activate, providing an inadequate reprogramming condition. Declarant Polejaeva does

not address rat oocyte spontaneous activation nor does applicant. Declarant's statement regarding rats, is nuclear transfer to produce rats is inefficient (parag. 21). Further, neither applicant nor Declarant offers any evidence to refute the findings of Fitchev that nuclear transfer in rats is unpredictable without the use of MG132 to prevent spontaneous oocyte activation. All that is offered is applicant's and declarant's opinion, without arguments or evidence directed to the data presented by Fitchev.

With specific attention to mice, applicant argues Wakayama practiced delayed activation as taught in the specification. Applicant argues Wakayama activated reconstructed oocytes after chromosome condensation, and that this process occurred within one hour of injection. Applicant argues this mirrors the guidance of the present specification which states to incubate between nucleus transfer and activation for a time not less that that which allowed chromosome formation and not long enough for spontaneous activation or death of the reconstructed oocytes. Applicant further argues Ogura teaches only delayed activation ultimately is important for successful mouse SCNT, and this is taught by the present specification. These arguments are not persuasive.

While Wakayama did incubate reconstructed oocytes, enucleated mouse oocytes having a mouse somatic or differentiated cell nucleus injected into it, for 1-6 hours prior to activation, the present specification makes no specific mention that for mice, any alteration to the period of time between reconstruction and activation would be necessary. The specific mention of delayed activation is made in general, but with specific reference to bovines (specification, pages 12-13, bridg. parag.). Further, the

specification states during such incubation the reconstructed oocytes need to be incubated in the presence of a microtubule destabilizer, exemplifying nocodazole, to promoter proper ploidy of the resulting embryos (specification, page 14, lines 18-17). Nocodazole accomplishes this by inhibiting formation of multiple nuclei according to the specification. Thus, from the specification, the skilled artisan would have thought the need was to disrupt microtubule organization to prevent the formation of multiple nuclei. Wakayama incubates the reconstructed mouse oocytes in media containing cytochalasin B prior to activation. Cytochalasin B inhibits microfilament organization, which prevents cytokinesis or the separation of a cell at the point in mitosis for the production of daughter cells (Wakayama (1998), page 373, col. 1, lines 1-4 and col. 2, parag. 1, lines 3-6). Applicant's specification would not have motivated the skilled artisan at the time of filing to inhibit cytokinesis, but polar body extrusion. Therefore, the methods of Wakayama for producing mice by nuclear transfer are materially different and separate from the methods disclosed by the present specification. While the present specification teaches delayed activation, the present specification teaches such to inhibit polar body exclusion and to induce the proper ploidy in resultant embryos, and not to inhibit cytokinesis as taught by Wakayama (1998). Ogura may state cytochalasin B treatment is not crucial for the production of cloned mice (Ogura, page 57, col. 2, parag. 2, lines 15-18), but a reading of Wakayama (1999), cited by Ogura, shows qualifiers to this statement not suggested by the present specification. The cells used in Wakayama (1999)'s production of mice were first of all ES cells, which are embryonic cells and specifically excluded by the claims. ES cells are thought to be more easily

reprogrammed than somatic cells, thus, inherently being more successful in directing the development of cloned animals. Thus, the statement in Ogura that cytochalasin B is not a crucial element for the production of clone mice, is based on data obtained using ES cells as nuclear donor, not somatic or differentiated cells as presently disclosed, and as taught by Wakayama (1998). This is a material difference. Thus there is no evidence that following the method disclosed in the present specification, at the time of filing, the skilled artisan would have been able to produce cloned mice. Based on the evidence of record, the method of Wakayama, requiring materially different protocols lacking basis in the present specification, would be effective in cloning mice from somatic or differentiated cell nuclei.

In regards to the cloning of rabbits, applicant argues the art taught at the time of filing, for transferred rabbit embryos to develop to term, the recipient female rabbit had to be asynchronous to the oocyte. Applicant argues the rabbit embryos of Landa and Al-Hasani were in vitro manipulated embryos, just as SCNT embryos would be. Further applicant argues Chesne states it would have been importing for the skilled artisan to take into account physiological features of rabbit embryos from the work of others. These arguments are not persuasive.

While the embryos of the present invention are indeed in vitro manipulated, the embryos of Landa and Al-Hasani are in vitro manipulated in materially different and separate ways. The mythologies of nuclear transfer, of the present invention, and embryo transfer of Landa or Al-Hasani, are not co-extensive. Landa transferred to asynchronous female rabbit recipients in situ produced embryos isolated from a rabbits

reproductive tract and Al-Hasani transferred to asynchronous female rabbits IVF rabbit embryos. Thus, the extent and type of manipulations are extremely different. Further, there is no guidance in the specification to use embryo transfer methodology from other animal husbandry applications. Much less there is no guidance to use asynchronous female rabbits as reconstituted rabbit embryo recipients. A novel method requires more disclosure than an invention which an improvement of a known method. Chesne is post-filing, and thus, comments about the work of others are not limited to work prior to the present effective filing date. One of skill in the art does not need to wait post-filing guidance for the presently claimed invention to become enabled. Chesne states there were no clone rabbits produced by nuclear transfer prior to their experiments. Thus, Chesne modified appellant's method using a protocol not suggested by applicant, and doing so produced cloned rabbits.

For rat nuclear transfer, applicant argues the problem and solution to spontaneous activation of rat oocytes had been addressed in the art prior to the time of filing. Applicant argues Keefer (1982) noted the spontaneous activation of in vitro cultured rat oocyte. Applicant also argues Keefer teaches rat oocytes need to be removed from culture as quickly as possible to avoid spontaneous activation. Applicant also argues from Keefer the skilled artisan would know to obtain MII rat oocytes, spontaneous activation would need to be avoided. These arguments are not persuasive.

Zhou states nuclear transfer (cloning) in rats "all previous attempts to clone rats have been unsuccessful, with developmental arrest at implantation stage" (Zhou, page

1179, col. 1, parag. 1, lines 11-15). Further, Zhou outlines acknowledges the issue of spontaneous activation of rat oocytes (page 1179, col. 1, parag. 2, lines 5-12), and teaches two methods to solve the issue (page 1179, col., parag. 2, lines 13-19 and line 31 to col. 2, line 6). Both of these experiments failed to produce cloned rats. The only method that was successful required the isolation of rat oocytes in the presence of a protease inhibitor (page 1179, col. 3, lines 1-5). Keefer, it is noted does not offer any guidance on inhibiting the spontaneous activation of rat oocytes, only warning of the danger this may pose to fertilizability of rat oocytes. The present specification contains no guidance on obviating this issue in rats. As such, the successful cloning of rats requires methodology not present in the specification.

For claims to horses produced by SCNT, applicant argues the boards emphasis on the time that had passed from this applications effective filing date to the first cloned horse does not equate with a lack of enablement. Applicant argues the availability of oocytes is a major factor in the cloning of horses. Applicant argues Lagutina states the position of the horse's ovaries makes them a poor oocyte donor. Applicant argues the techniques cited in Galli, inhibition of both protein synthesis and protein phosphorylation, and zona free manipulation are not critical for horse cloning. Applicant argues Hinrichs (1995) teaches 49% activation of equine oocytes when the oocytes are incubated with a proteins synthesis inhibition alone. Likewise, applicant argues equine oocytes were activated in the presence of a protein synthesis inhibitor alone but rose to 93% when both a protein synthesis inhibitor and protein phosphorylation inhibitor were used. Applicant argues increasing the number of activated oocytes would be only one

way to increase nuclear transfer efficiency, but increasing the absolute number of nuclear transfer embryos would also increase efficiency. Thus, increasing the number of oocytes activated is not necessary. Applicant argues Lagutina teaches the zona-free method for embryo reconstruction proved very efficient increasing the fusion rate and lead to an efficient use of oocytes. Applicant argues efficient is not the same as critical. Applicant offers as further evidence, the cloning of a mule using horse oocytes in embryo reconstruction, where zona enclosed oocytes were used, indicating zona free oocytes are not critical to the cloning of horses. These arguments are not persuasive.

Lagutina states (page 560, parag. 2, lines 1-9:

> The refinement of the in vitro culture conditions suitable for equine oocyte maturation and embryo development (Galli et al. 2002a, Lazzari et al. 2002a), the development of an adequate horse oocyte activation protocol (Lazzari et al. 2002b) and the application of zona-free manipulation for embryo reconstruction (Booth et al. 2001, Oback et al. 2003, Vajta et al. 2003), are all *fundamental* steps for the development of a successful in vitro procedure for somatic cell nuclear transfer in the horse. (Emphasis added).)

The fundamental steps of Lagutina are zona free manipulations, and inhibition of protein synthesis (cycloheximide) and protein phosphorylation (6DMAP) during activation (page 561, col. 1, parag. 3 and col. 2, parag. 1). Thus, Lagutina supports the statements of Galli (2003) of record that these “aides” increased efficiency so that SCNT for cloning horses could be successful, that a live-born horse. The present specification does not offer any guidance for zona free manipulation of embryos or inhibition of both protein synthesis and protein phosphorylation. Thus, the production of cloned horses required a novel protocol unsupported by the present specification.

Hinrichs does not overcome the teachings of Galli (2003) or Lagutina (2005). Hinrichs only studied horse oocyte activation, without the formation of embryos or performing any embryo transfer. Further, Hinrichs provides no evidence a more efficient method of activating horse oocytes would necessarily lead to more cloned horses. As known in the art, and evidence by Pennisi et al, even pregnancy does not lead to a live-born clone (Pennisi and Vogel (2000), page 1722, col. 1, parag. 3, lines 16-18). Thus, by extension, activated oocytes would not have been regarded by the skilled artisan at the time of filing to necessarily lead to a cloned mammal.

Applicant concludes by arguing the BPAI's decision was based on deeming non-cirtical additions to the method disclosed in the present specification to be critical for enablemnet of the claimed cloned mice, rabbits, horses and rats. Applicant argues many of the variations used in the cited references were simply applying techniques know for in vitro manipulated rabbit embryos or well known techniques for harvesting rat oocytes. Applicant argues repetition of the presently disclosed method of nuclear transfer to produce cloned mice, rabbits, horses and rats does not equate with undue experimentation if all that is required is repetition. These arguments are not persuasive.

As provided above, the methodology ultimately successful in the cloning of mice, rabbits, horse and rats required methodology not taught in the art to be relevant to SCNT of the particular species. Furthermore, the specification failed to provide any guidance to any of the successful methodology either in general or specifically towards mice, rabbits, horses or rats. Thus, the post-filing successes for these animals required

the development and implementation of novel methods not supported by the specification or the art at the time of filing. While the level of experimentation is extremely high in SCNT, the level of guidance required for enablement at the time of filing (1995) is also very high. The specification, thus, fails to supply guidance for the cloning of mice, rabbits, horses or rats. Additionally, declarant Polejaeva had directed specific comments only to the cloning by SCNT of pigs. All other opinions are general and lack any specific evidence towards SCNT for the cloning of mice, rabbits, horses or rats.

In the art rejections below, the rejections have been made under 35 U.S.C. § 102/103. The phrase "live-born clone of a … mammal" imbues the method by which the clone was made, nuclear transfer.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skills in the art to which said subject matter pertains. patentability shall not be negatived by the manner in which the invention was made.

Claims 163 and 168 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Eppig et al. (1989) Biology of Reproduction, Vol. 41, pp. 268-276.

Eppig teaches live-born mice produced by in vitro fertilization (IVF) (peg 274, col. 1, parag. 2 to col. 2, line 5).

As the presently claimed cloned mice are not taught nor claimed to exhibit a novel structural or functional difference from the mice produced by IVF, described in Eppig, Eppig anticipates the claimed invention. In the alternative, the claimed mice are obvious over Eppig because there is no structural or functional difference between the claimed sheep and the sheep of Eppig. If there are any such structural characteristics or features that would distinguish the claimed mice from those of Eppig, applicant should note them. While the mice of Eppig and those claimed are produced by materially different and separate methods, there is no evidence of record or in the art that the method of making the mice, nuclear transfer verses IVF, offers any distinguishing structure, feature or characteristic.

Further, declarant Polejaeva states clones have the same genetic complement as that of the donor nucleus (Declaration, filed March 30, 2008, parag. 95), but what is meant by genetic complement is not clear. The term is not defined by the specification or by declarant, but is taken to mean the same assortment of genes, regulatory sequences, intervening sequences and junk DNA. However, by having the same complement, this is not taken to be the nucleotide sequence of the genome is identical between the clone and the nucleus donor animal. It is noted in early prosecution,

applicant argued the clone and the donor were "genetically identical." Thus, a clone and the donor are not exactly the same. Therefore, the issue remains as to how to distinguish a clone and the donor. This issue leads to the present art rejection. If one presents two mice, there is no means by which to tell the cloned mouse from the IVF produced mouse of Eppig.

Applicant continues to argue the fact that the clone has the same genetic complement as the donor is a distinguishing structural feature. However, applicant still fails to state a method by which to make such a distinction. If we have two mice, what test does one use to tell which one was produced by nuclear transfer as presently claimed, that is a cloned mouse, from the mouse produced by IVF? The specification does not teach any such method, and applicant has not replied specifically to a request to state on the record how to distinguish between a known mouse and a live born mouse clone. Additionally, Declarant Polejaeva does not provide any evidence, method or statement that a clone is distinguishable from an animal of the same species produced by a different method.

With being able to distinguish between the claimed clone and the mouse of Eppig, applicant's mouse is an old product, produced by a new method. Just as an IVF produced mouse is not patentable over a wild-type mouse, the cloned mouse is not patentable over the IVF produced mouse because there are no new structures imbued by the cloning method so that the cloned mouse has patentable distinction over the IVF produced mouse. Without distinction over a known mouse, applicant's presently cloned mouse is not patentable. A new method of making an old product simply does not

provide patentability to the product made by the new method. The mice claimed and those of Eppig are the same or are obvious variants over one another because of the epigenetic effects discussed by declarant (Declaration, filed March 30, 2008, parag. 95).

Thus, Eppig either anticipates or makes obvious the claimed invention.

Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the *prima facie* case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433. See also *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985), *In re Ludtke*, 441 F.2d 660, 169 USPQ 563 (CCPA 1971), *Northam Warren Corp. v. D. F. Newfield Co.*, 7 F. Supp. 773, 22 USPQ 313 (E.D.N.Y. 1934) and MPEP 2112.01.

Claims 163 and 169 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Brackett et al. (1975) Biology of Reproduction, Vol. 12, pages 260-274.

Brackett teaches live-born rabbits produced by in vitro fertilization (IVF) (page 269, col. 2, lines 9-15).

As the presently claimed cloned rabbits are not taught nor claimed to exhibit a novel structural or functional difference from the rabbits produced by IVF, described in Brackett, Brackett anticipates the claimed invention. In the alternative, the claimed rabbits are obvious over Brackett because there is no structural or functional difference between the claimed rabbit and the rabbit of Brackett. If there are any such structural characteristics or features that would distinguish the claimed rabbits from those of

Brackett, applicant should note them. While the rabbits of Brackett and those claimed are produced by materially different and separate methods, there is no evidence of record or in the art that the method of making the rabbits, nuclear transfer verses IVF, offers any distinguishing structure, feature or characteristic.

Further, declarant Polejaeva states clones have the same genetic complement as that of the donor nucleus (Declaration, filed March 30, 2008, parag. 95), but what is meant by genetic complement is not clear. The term is not defined by the specification or by declarant, but is taken to mean the same assortment of genes, regulatory sequences, intervening sequences and junk DNA. However, by having the same complement, this is not taken to be the nucleotide sequence of the genome is identical between the clone and the nucleus donor animal. It is noted in early prosecution, applicant argued the clone and the donor were "genetically identical." Thus, a clone and the donor are not exactly the same. Therefore, the issue remains as to how to distinguish a clone and the donor. This issue leads to the present art rejection. If one presents two rabbits, there is no means by which to tell the cloned rabbit from the IVF produced rabbit of Brackett.

Applicant continues to argue the fact that the clone has the same genetic complement as the donor is a distinguishing structural feature. However, applicant still fails to state a method by which to make such a distinction. If we have two rabbits, what test does one use to tell which one was produced by nuclear transfer as presently claimed, that is a cloned rabbit, from the rabbit produced by IVF? The specification does not teach any such method, and applicant has not replied specifically to a request to

state on the record how to distinguish between a known rabbit and a live born rabbit clone. Additionally, Declarant Polejaeva does not provide any evidence, method or statement that a clone is distinguishable from an animal of the same species produced by a different method.

With being able to distinguish between the claimed clone and the rabbit of Brackett, applicant's rabbit is an old product, produced by a new method. Just as an IVF produced rabbit is not patentable over a wild-type rabbit, the cloned rabbit is not patentable over the IVF produced rabbit because there are no new structures imbued by the cloning method so that the cloned rabbit has patentable distinction over the IVF produced rabbit. Without distinction over a known rabbit, applicant's presently cloned rabbit is not patentable. A new method of making an old product simply does not provide patentability to the product made by the new method. The rabbits claimed and those of Brackett are the same or are obvious variants over one another because of the epigenetic effects discussed by declarant (Declaration, filed March 30, 2008, parag. 95).

Thus, Brackett either anticipates or makes obvious the claimed invention.

Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the *prima facie* case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433. See also *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985), *In re Ludtke*, 441 F.2d 660, 169 USPQ 563 (CCPA 1971), *Northam Warren Corp. v. D. F. Newfield Co.*, 7 F. Supp. 773, 22 USPQ 313 (E.D.N.Y. 1934) and MPEP 2112.01.

Claims 163 and 170 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Palmer et al. (1991) Journal of Reproduction and Fertility Supplement, Vol. 44, pages 375-384.

Palmer teaches the production of live-born horses by in vitro fertilization (IVF) (page 382, parag. 2).

As the presently claimed cloned horses are not taught nor claimed to exhibit a novel structural or functional difference from the horses produced by IVF, described in Palmer, Palmer anticipates the claimed invention. In the alternative, the claimed horses are obvious over Palmer because there is no structural or functional difference between the claimed horses and the horse of Palmer. If there are any such structural characteristics or features that would distinguish the claimed horses from those of Palmer, applicant should note them. While the horse of Palmer and those claimed are produced by materially different and separate methods, there is no evidence of record or in the art that the method of making the horses, nuclear transfer verses IVF, offers any distinguishing structure, feature or characteristic.

Further, declarant Polejaeva states clones have the same genetic complement as that of the donor nucleus (Declaration, filed March 30, 2008, parag. 95), but what is meant by genetic complement is not clear. The term is not defined by the specification or by declarant, but is taken to mean the same assortment of genes, regulatory sequences, intervening sequences and junk DNA. However, by having the same complement, this is not taken to be the nucleotide sequence of the genome is identical between the clone and the nucleus donor animal. It is noted in early prosecution,

applicant argued the clone and the donor were "genetically identical." Thus, a clone and the donor are not exactly the same. Therefore, the issue remains as to how to distinguish a clone and the donor. This issue leads to the present art rejection. If one presents two horses, there is no means by which to tell the cloned horse from the IVF produced horse of Palmer.

Applicant continues to argue the fact that the clone has the same genetic complement as the donor is a distinguishing structural feature. However, applicant still fails to state a method by which to make such a distinction. If we have two horses, what test does one use to tell which one was produced by nuclear transfer as presently claimed, that is a cloned horse, from the horse produced by IVF? The specification does not teach any such method, and applicant has not replied specifically to a request to state on the record how to distinguish between a known horse and a live born horse clone. Additionally, Declarant Polejaeva does not provide any evidence, method or statement that a clone is distinguishable from an animal of the same species produced by a different method.

With being able to distinguish between the claimed clone and the horse of Palmer, applicant's horse is an old product, produced by a new method. Just as an IVF produced horse is not patentable over a horse produced by mating, the cloned horse is not patentable over the IVF produced horse because there are no new structures imbued by the cloning method so that the cloned horse has patentable distinction over the IVF produced horse. Without distinction over a known horse, applicant's presently cloned horse is not patentable. A new method of making an old product simply does not

provide patentability to the product made by the new method. The horses claimed and those of Palmer are the same or are obvious variants over one another because of the epigenetic effects discussed by declarant (Declaration, filed March 30, 2008, parag. 95).

Thus, Palmer either anticipates or makes obvious the claimed invention.

Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the *prima facie* case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433. See also *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985), *In re Ludtke*, 441 F.2d 660, 169 USPQ 563 (CCPA 1971), *Northam Warren Corp. v. D. F. Newfield Co.*, 7 F. Supp. 773, 22 USPQ 313 (E.D.N.Y. 1934) and MPEP 2112.01.

Claims 163 and 171 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Toyoda et al. (1974) Journal of Reproduction and Fertility, Vol. 36, pages 9-22.

Toyoda teaches the production of live-born rats by in vitro fertilization (IVF) (page 19, parag. 1, lines 1-4).

As the presently claimed cloned rats are not taught nor claimed to exhibit a novel structural or functional difference from the rats produced by IVF, described in Toyoda, Toyoda anticipates the claimed invention. In the alternative, the claimed rats are obvious over Toyoda because there is no structural or functional difference between the claimed rats and the rat of Toyoda. If there are any such structural characteristics or features that would distinguish the claimed rats from those of Toyoda, applicant should

note them. While the rat of Toyoda and those claimed are produced by materially different and separate methods, there is no evidence of record or in the art that the method of making the rats, nuclear transfer verses IVF, offers any distinguishing structure, feature or characteristic.

Further, declarant Polejaeva states clones have the same genetic complement as that of the donor nucleus (Declaration, filed March 30, 2008, parag. 95), but what is meant by genetic complement is not clear. The term is not defined by the specification or by declarant, but is taken to mean the same assortment of genes, regulatory sequences, intervening sequences and junk DNA. However, by having the same complement, this is not taken to be the nucleotide sequence of the genome is identical between the clone and the nucleus donor animal. It is noted in early prosecution, applicant argued the clone and the donor were "genetically identical." Thus, a clone and the donor are not exactly the same. Therefore, the issue remains as to how to distinguish a clone and the donor. This issue leads to the present art rejection. If one presents two rats, there is no means by which to tell the cloned rat from the IVF produced rat of Toyoda.

Applicant continues to argue the fact that the clone has the same genetic complement as the donor is a distinguishing structural feature. However, applicant still fails to state a method by which to make such a distinction. If we have two rats, what test does one use to tell which one was produced by nuclear transfer as presently claimed, that is a cloned rat, from the rat produced by IVF? The specification does not teach any such method, and applicant has not replied specifically to a request to state

on the record how to distinguish between a known rat and a live born rat clone. Additionally, Declarant Polejaeva does not provide any evidence, method or statement that a clone is distinguishable from an animal of the same species produced by a different method.

With being able to distinguish between the claimed clone and the rat of Toyoda, applicant's rat is an old product, produced by a new method. Just as an IVF produced rat is not patentable over a rat produced by mating, the cloned rat is not patentable over the IVF produced rat because there are no new structures imbued by the cloning method so that the cloned rat has patentable distinction over the IVF produced rat. Without distinction over a known rat, applicant's presently cloned rat is not patentable. A new method of making an old product simply does not provide patentability to the product made by the new method. The rats claimed and those of Toyoda are the same or are obvious variants over one another because of the epigenetic effects discussed by declarant (Declaration, filed March 30, 2008, parag. 95).

Thus, Toyoda either anticipates or makes obvious the claimed invention.

Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the *prima facie* case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433. See also *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985), *In re Ludtke*, 441 F.2d 660, 169 USPQ 563 (CCPA 1971), *Northam Warren Corp. v. D. F. Newfield Co.*, 7 F. Supp. 773, 22 USPQ 313 (E.D.N.Y. 1934) and MPEP 2112.01.

With regard to prior rejections made under 35 U.S.C. § 102/103, applicant argues for anticipation the identical invention must be shown in as complete details as contained in the patent claims and requires the presence in a single prior art disclosure all the elements of a claimed invention. Applicant argues, generally, the prior art did not show the production of a clone of a pre-existing, non-embryonic donor mammal. Applicant argues this omission in the prior art precludes the present claims from being anticipated. Applicant further argues the mammals in the prior art would have the genetic complement of two parents, not just one, the parent being the nuclear donor. These arguments are not persuasive.

The rejection here is based on patentably indistinctness between the claimed clones of pre-existing mice, rabbits, horses and rats. There is no disclosure in the present specification that directs the determination of a cloned mouse, rabbit, horse or rat from those of the cited prior art. Neither the specification disclose any new feature or characteristic of the cloned mice, rabbits, horses, and rats from those made by IVF. As such applicant's clones are the same as the mammals known in the art at the time of filing. Applicant has a new method for producing an old product. While having been made by a method of nuclear transfer (cloning) enables the art to produce inexact copies of pre-existing mammals, the method does not alter the mammal itself. The statements made by declarant, relate to the method, not the mammal. Coexistence, time-delayed, inexact copy are all traits of the method. The mammal produced by such a method cannot be distinguished from any other wild type mammal of the same species. Applicant should clearly state how such a distinction can be made. The only

imaginable means to make a distinction would be to review breeding records to determine how the mouse, rabbit, horse or rat was produced. This, however, does not impart a novel trait the mouse, rabbit, horse or rat in question.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is (571)272-0727. The examiner can normally be reached on M-Fri, 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Deborah Crouch/
Primary Examiner, Art Unit 1632

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